Stroke Note

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Dissolution of the Left Atrial Appendage Thrombus with Rivaroxaban Therapy

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Introduction

Because patients with ischemic stroke and atrial fibrillation (AF) have an increased risk of recurrent embolism, they should receive anticoagulant therapy [1]. In patients with AF, thrombi usually form in the left atrium (LA) and left atrial appendage (LAA), so detection of LA/LAA thrombus may help to identify patients with a high risk of recurrent stroke.

Serial transesophageal echocardiography (TEE) has demonstrated the dissolution of intracardiac thrombi with anticoagulant therapy [2, 3]. Recently, novel oral anticoagulants (NOACs) have emerged as alternative prophylaxis for thromboembolism in patients with nonvalvular AF. However, the effect of NOACs on intracardiac thrombi has not been fully elucidated. Here we report on the dissolution of LAA thrombus in 3 patients with nonvalvular AF-related stroke receiving rivaroxaban. The clinical and neuroradiological characteristics of the 3 patients are summarized in table 1.

Case 1

An 81-year-old woman presented to our hospital with left hemiparesis. Brain magnetic resonance imaging (MRI) revealed acute infarction in the right middle cerebral artery (MCA) territory, and the electrocardiogram (ECG) showed AF. Intravenous unfractionated heparin (UFH) was administered and was switched to rivaroxaban (10 mg/day) on day 3. TEE demonstrated LAA thrombus (18 × 7 mm) on day 4. This was reduced in size (12 × 9 mm) on day 23, and resolved on day 35 (fig. 1).

Case 2

A 75-year-old man presented to our hospital with left arm weakness. He had a history of paroxysmal AF, but was not on anticoagulant therapy. Brain MRI revealed acute infarction in the

Table 1. Clinical and neuroradiological characteristics

	Case 1	Case 2	Case 3
Age, years	81	75	75
Sex	F	M	M
Onset to admission time	20 h	9 h	unknown
Neurological symptoms	dysarthria, hemiparesis	dysarthria, hemiparesis	aphasia, hemiparesis
NIHSS score on admission	6	4	7
MRI on admission			
Acute infarcts on DWI	the right basal ganglia, insular cortex and corona radiate	the bilateral frontal and the right parietal cerebral cortex	the left insular cortex, frontal and temporal cerebral cortex
T2*-WI	no CMBs	no CMBs	not done
MRA on admission	occlusion at the right distal MCA	no occlusion/stenosis	occlusion at the left proximal MCA
Thrombolysis	not done	not done	not done
Initial therapy	intravenous UFH	intravenous UFH	intravenous UFH
Follow-up MRI	no new lesions (day 37)	no new lesions (day 8)	enlargement of infarction in the left temporal lobe, hemorrhagic infarction in the left putamen (day 5)
Follow-up MRA	recanalization of the left MCA (day 37)	no occlusion/stenosis (day 8)	partial recanalization of the left MCA (day 5)
Initiation of rivaroxaban	day 3	day 3	day 12
TEE examinations	days 4, 23 and 35	days 3 and 10	days 13 and 19
A-S-C-O classification	A0-S0-C1-O0	A2-S0-C1-O0	A2-S0-C1-O0
mRS score at discharge	1	1	2

NIHSS = National Institutes of Health Stroke Scale; DWI = diffusion-weighted imaging; CMBs = cerebral microbleeds; MRA = magnetic resonance angiography; mRS = modified Rankin Scale.

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bilateral cerebral hemispheres, and he was given intravenous UFH. TEE revealed LAA thrombus (10 × 34 mm) and rivaroxaban (10 mg/day) was started on day 3. Follow-up TEE showed disappearance of the thrombus on day 10 (fig. 1).

Case 3

A 75-year-old man presented to our hospital with aphasia and right hemiparesis. Brain MRI revealed acute infarction in the left MCA territory and ECG monitoring detected paroxysmal AF. He initially received intravenous UFH, and was switched to rivaroxaban (10 mg/day) on day 12. TEE detected LAA thrombus (8 × 21 mm) on day 13, which resolved by day 19 (fig. 1).

Discussion

Several authors have reported the dissolution of LAA thrombi in patients treated with oral warfarin [2, 3]. The mechanism of thrombolysis is thought to involve relative predominance of plasma fibrinolytic activity over thrombin activity [4]. Heparin administration can be considered for acute ischemic stroke in Japanese guidelines [5]. However, TEE detected LAA thrombus during heparin administration in our 3 cases. There have been few recent reports about the resolution of LAA thrombus in patients treated with NOACs [6, 7]. In our cases, TEE showed disappearance of thrombi after 1–5 weeks of rivaroxaban treatment without recurrent stroke.

Rivaroxaban is a direct factor Xa inhibitor that efficiently blocks the generation of thrombin [8]. By decreasing thrombin production, rivaroxaban causes a looser clot to form that is more sensitive to fibrinolytic enzymes [9], which may explain its efficacy in promoting the dissolution of LAA thrombus. Low-dose rivaroxaban (10 mg/day) is approved for patients with renal dysfunction in Japan [10], and even it can dissolve LAA thrombus. In the future, the fibrinolytic effect of NOACs on intracardiac thrombi in patients with acute cardioembolic stroke should be clarified by larger studies.

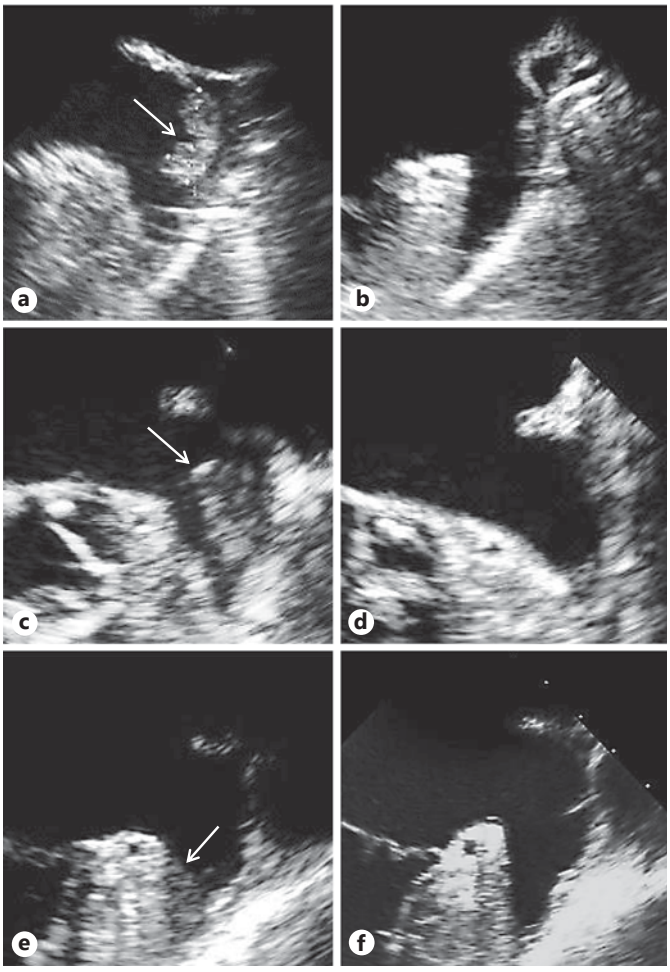

Fig. 1. TEE in cases 1 (**a**, **b**), 2 (**c**, **d**) and 3 (**e**, **f**). In case 1, LAA thrombus (arrow) was observed 1 day after the initiation of rivaroxaban (**a**). It disappeared after 32 days of rivaroxaban treatment (**b**). In case 2, TEE demonstrated LAA thrombus (arrow) before rivaroxaban treatment (**c**). After 7 days of rivaroxaban treatment TEE showed complete dissolution of the thrombus (**d**). In case 3, TEE revealed LAA thrombus (arrow) 1 day after initiation of rivaroxaban (**e**). Dissolution of the thrombus was achieved after 7 days of rivaroxaban treatment (**f**).

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References

1 European Atrial Fibrillation Trial Study Group: Secondary prevention in non-rheumatic atrial fibrillation after transient ischaemic attack or minor stroke. Lancet 1993;342:1255–1262.
2 Collins LJ, Silverman DI, Douglas PS, Manning WJ: Cardioversion of nonrheumatic atrial fibrillation: reduced thromboembolic complications with 4 weeks of precardioversion anticoagulation are related to atrial thrombus resolution. Circulation 1995;92:160–163.
3 Jaber WA, Prior DL, Thamilarasan M, Grimm RA, Thomas JD, Klein AL, Asher CR: Efficacy of anticoagulation in resolving left atrial and left atrial appendage thrombi: a transesophageal echocardiographic study. Am Heart J 2000;140:150–156.
4 Yasaka M, Yamaguchi T, Miyashita T, Tsuchiya T: Regression of intracardiac thrombus after embolic stroke. Stroke 1990;21:1540–1544.
5 Kern R, Nagayama M, Toyoda K, Steiner T, Hennerici MG, Shinohara Y: Comparison of the European and Japanese guidelines for the management of ischemic stroke. Cerebrovasc Dis 2013;35:402–418.
6 Vidal A, Vanerio G: Dabigatran and left atrial appendage thrombus. J Thromb Thrombolysis 2012;34:545–547.
7 Hammerstingl C, Potzsch B, Nickenig G: Resolution of giant left atrial appendage thrombus with rivaroxaban. Thromb Haemost 2013;109:583–584.
8 Gerotziafas GT, Elalamy I, Depasse F, Perzborn E, Samama MM: In vitro inhibition of thrombin generation, after tissue factor pathway activation, by the oral, direct factor Xa inhibitor rivaroxaban. J Thromb Haemost 2007;5:886–888.
9 Varin R, Mirshahi S, Mirshahi P, Klein C, Jamshedov J, Chidiac J, Perzborn E, Mirshahi M, Soria C, Soria J: Whole blood clots are more resistant to lysis than plasma clots – greater efficacy of rivaroxaban. Thromb Res 2013;131:100–109.
10 Hori M, Matsumoto M, Tanahashi N, Momomura S, Uchiyama S, Goto S, Izumi T, Koretsune Y, Kajikawa M, Kato M, Ueda H, Iwamoto K, Tajiri M, J-ROCKET AF Study Investigators: Rivaroxaban versus warfarin in Japanese patients with atrial fibrillation – the J-ROCKET AF study. Circ J 2012;76:2104–2111.